

CLAIMS

1. A method for determining the presence of at least one analyte, comprising:  
providing a sample comprising a plurality of aggregates of size of at least about 500  
5 nm adsorbing a plurality of analytes;  
exposing the sample to electromagnetic radiation to cause surface-enhanced emission;  
obtaining spectral information of the sample, wherein at least one spectral line of the  
information represents a single analyte adsorbed on one of the plurality of aggregates; and  
determining the presence of the single analyte from the at least one spectral line.  
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2. A method as in claim 1, the exposing step involving exposing the sample to  
electromagnetic radiation and causing Raman scattering of the sample, and the obtaining step  
comprising obtaining Raman information of the sample, wherein a single Raman line of the  
information represents the single analyte.  
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3. A method as in claim 1, wherein the sample is free of an emission-enhancing aid.
4. A method as in claim 1, wherein the spectral information is a surface-enhanced  
Raman spectrum, having an enhancement factor of at least about  $10^{10}$ .  
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5. A method as in claim 1, wherein each aggregate of the plurality of aggregates  
comprises a plurality of metal particles.
6. A method as in claim 5, wherein the plurality of metal particles is selected from the  
25 group consisting of silver, gold and copper particles.
7. A method as in claim 6, wherein the aggregate is formed in situ by exposure to the  
electromagnetic radiation.
- 30 8. A method as in claim 1, wherein the plurality of aggregates is selected from the group  
consisting of colloids suspended in a medium, aggregates deposited on a substrate and  
lithography-produced metal aggregates.

9. A method as in claim 8, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.
10. A method as in claim 8, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.
11. A method as in claim 1, wherein the sample consists essentially of a plurality of aggregates of from about 500 nm to about 20 microns in dimension.
12. A method as in claim 1, wherein the electromagnetic radiation is non-resonant radiation.
13. A method as in claim 12, wherein the electromagnetic radiation is near infrared radiation.
14. A method as in claim 1, wherein the spectral information is Raman information that defines less than a complete Raman spectrum.
15. A method as in claim 14, wherein the spectral information is less than 5 Raman lines.
16. A method as in claim 14, wherein the spectral information is less than 2 Raman lines.
17. A method as in claim 1, wherein the spectral information is a single Raman line.
18. A method as in claim 1, wherein the single analyte is a dye.
19. A method as in claim 1, wherein the single analyte is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.
20. A method as in claim 1, wherein the single analyte is selected from the group consisting of nucleotides and nucleosides.
21. A method as in claim 1, wherein the single analyte is a therapeutic agent.

22. A method as in claim 1, wherein the single analyte is a neurotransmitter.
23. A method for determining the presence of an analyte, comprising:  
5 providing a sample comprising a plurality of aggregates adsorbing a plurality of analytes, wherein at least one aggregate of the plurality of aggregates comprises a metal cluster of at least seven particles and adsorbs only one analyte;  
exposing the sample to electromagnetic radiation to cause surface-enhanced emission;  
obtaining spectral information of the sample, wherein the only one analyte contributes  
10 to the spectral information; and  
determining the presence of the only one analyte from the spectral information.
24. A method as in claim 23, the exposing step involving exposing the sample to electromagnetic radiation to cause Raman scattering, and the obtaining step involves  
15 obtaining a Raman spectrum of the sample, wherein the only one analyte contributes to at least one Raman signal of the Raman spectrum.
25. A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster of at least ten particles.  
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26. A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster of at least twenty particles.
27. A method as in claim 23, wherein the plurality of aggregates comprises a metal cluster  
25 of at least thirty-five particles.
28. A method as in claim 23, wherein the sample is free of an emission-enhancing aid.
29. A method as in claim 23, wherein the Raman spectrum is a surface-enhanced Raman  
30 spectrum, having an enhancement factor of at least 1010.
30. A method as in claim 23, wherein the metal particles are selected from the group consisting of silver, gold and copper particles.

31. A method as in claim 23, wherein the aggregate is formed in situ by exposure to the electromagnetic radiation.
- 5 32. A method as in claim 23, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.
33. A method as in claim 32, wherein the medium is selected from the group consisting of  
10 water, an organic solvent and a gel.
34. A method as in claim 32, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.
- 15 35. A method as in claim 23, wherein the at least one aggregate has a dimension of at least about 500 nm.
36. A method as in claim 23, wherein the electromagnetic radiation is non-resonant radiation.  
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37. A method as in claim 36, wherein the electromagnetic radiation is near infrared radiation.
38. A method as in claim 23, wherein the single analyte is a dye.  
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39. A method as in claim 23, wherein the single analyte is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.
40. A method as in claim 23, wherein the single analyte is selected from the group  
30 consisting of nucleotides and nucleosides.
41. A method as in claim 23, wherein the single analyte is a therapeutic agent.

42. A method as in claim 23, wherein the single analyte is a neurotransmitter.

43. A method as in claim 23, wherein the sample consists essentially of aggregates of size of from about 500 nm to about 20 microns.

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44. A method as in claim 23, wherein the at least one aggregate comprises a plurality of metal particles each having a dimension of no more than about 100 nm.

45. A method as in claim 23, wherein the at least one aggregate comprises a plurality of metal particles each having a dimension of no more than about 75 nm.

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46. A method for determining the presence of an analyte, comprising:

providing a sample comprising a plurality of aggregates adsorbing a plurality of analytes, wherein each aggregate comprises a plurality of metal particles, each metal particle having a dimension of no more than about 100 nm and at least one aggregate adsorbs only one analyte;

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exposing the sample to electromagnetic radiation to cause surface-enhanced emission; obtaining spectral information of the sample, wherein the only one analyte contributes to the spectral information; and

determining the presence of the only one analyte from the spectral information.

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47. A method as in claim 46, wherein the exposing step involves causing surface-enhanced emission and the obtaining step involves obtaining Raman spectral information.

48. A method as in claim 46, wherein the sample is free of an emission-enhancing aid.

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49. A method as in claim 46, wherein the spectral information is a surface-enhanced Raman spectrum, having an enhancement factor of at least 1010.

50. A method as in claim 46, wherein the metal particles are selected from the group consisting of silver, gold and copper particles.

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51. A method as in claim 46, wherein the aggregate is formed in situ by exposure to the

electromagnetic radiation.

52. A method as in claim 46, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

53. A method as in claim 52, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

54. A method as in claim 52, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

55. A method as in claim 46, each metal particle having a dimension of no more than about 75 nm.

56. A method as in claim 46, wherein the electromagnetic radiation is non-resonant radiation.

57. A method as in claim 56, wherein the electromagnetic radiation is near infrared radiation.

58. A method as in claim 46, wherein the spectral information consists essentially of less than 5 lines of a Raman spectrum.

59. A method as in claim 46, wherein the single analyte is a dye.

60. A method as in claim 46, wherein the single analyte is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

61. A method as in claim 46, wherein the single analyte is selected from the group consisting of nucleotides and nucleosides.

62. A method as in claim 46, wherein the single analyte is a therapeutic agent.

63. A method as in claim 46, wherein the single analyte is a neurotransmitter.
64. A method for determining the presence of at least one analyte, comprising:  
5 providing a sample comprising a plurality of aggregates, at least one aggregate adsorbing only one analyte that is free of an emission-enhancing aid;  
exposing the sample to electromagnetic radiation; and  
obtaining a spectrum, wherein the only one analyte contributes to at least one signal of  
the spectrum.  
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65. A method as in claim 64, wherein the spectrum is a surface-enhanced Raman spectrum, having an enhancement factor of at least 10<sup>10</sup>.
66. A method as in claim 64, wherein each aggregate of the plurality of aggregates  
15 comprises a plurality of metal particles.
67. A method as in claim 66, wherein the metal particles are selected from the group consisting of silver, gold and copper particles.
- 20 68. A method as in claim 64, wherein the plurality of aggregates is formed in situ by exposure to the electromagnetic radiation.
69. A method as in claim 64, wherein the plurality of aggregates is selected from the group consisting of a colloids suspended in a medium, aggregates deposited on a substrate  
25 and lithography produced metal aggregates.
70. A method as in claim 69, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.
- 30 71. A method as in claim 69, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.
72. A method as in claim 64, wherein the at least one aggregate has a dimension of at

least about 500 nm.

73. A method as in claim 64, wherein the single analyte is a dye.

5 74. A method as in claim 64, wherein the single analyte is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

75. A method as in claim 64, wherein the single analyte is selected from the group consisting of nucleotides and nucleosides.

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76. A method as in claim 64, wherein the single analyte is a therapeutic agent.

77. A method as in claim 64, wherein the single analyte is a neurotransmitter.

15 78. A method for determining the presence of a single analyte, comprising:  
providing a sample comprising a plurality of surfaces, a portion of the plurality of  
surfaces adsorbing only one analyte; and  
exposing the sample to electromagnetic radiation to cause the sample to emit radiation  
such that the sample is free of photobleaching.

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79. A method as in claim 78, wherein the plurality of surfaces comprises a plurality of  
aggregates.

25 80. A method as in claim 79, wherein the plurality of aggregates comprises a plurality of  
metal particles.

81. A method as in claim 80, wherein the metal particles are selected from the group  
consisting of silver, gold and copper particles.

30 82. A method as in claim 79, wherein the plurality of aggregates is selected from the  
group consisting of a colloids suspended in a medium, aggregates deposited on a substrate  
and lithography produced metal aggregates.



83. A method as in claim 82, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

84. A method as in claim 82, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

85. A method as in claim 78, wherein the plurality of surfaces comprises a plurality of aggregates of metal particles, each of the metal particles having a dimension of no more than about 100 nm.

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86. A method as in claim 78, wherein the only one analyte is a dye.

87. A method as in claim 78, wherein the only one analyte is selected from the group consisting of thymine, adenine, cytosine, guanine, and uracil.

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88. A method as in claim 78, wherein the only one analyte is selected from the group consisting of nucleotides and nucleosides.

89. A method as in claim 78, wherein the only one analyte is a therapeutic agent.

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90. A method as in claim 78, wherein the only one analyte is a neurotransmitter.

91. A method for determining the presence of at least one molecule, comprising providing at least one molecule, exposing the at least one molecule to electromagnetic radiation to cause Raman scattering, obtaining Raman spectral information and determining the presence of the at least one molecule from at least one anti-Stokes line.

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92. A method as in claim 91, wherein the at least one molecule is adsorbed on a plurality of surfaces.

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93. A method as in claim 91, wherein the at least one analyte is exposed to non-resonant radiation.

94. A method as in claim 92, wherein the electromagnetic radiation is near infrared radiation.

95. A method as in claim 94, wherein the near infrared radiation has a wavelength of at least 1000 nm.

96. A method for sequencing at least a portion of DNA or RNA, comprising:  
cleaving the at least a portion of DNA or RNA into DNA or RNA fragments, wherein each fragment comprises at least one base;  
allowing each DNA or RNA fragment to become surface-adsorbed;  
exposing each fragment to electromagnetic radiation to cause surface-enhanced emission; and  
obtaining unique surface-enhanced spectral information attributed to each fragment.

97. A method as in claim 96, wherein each fragment is surface-adsorbed onto one of a plurality of surfaces.

98. A method as in claim 97, wherein the plurality of surfaces is included in a moving stream.

99. A method as in claim 97, wherein the plurality of surfaces is selected from the group consisting of a plurality of aggregates suspended in a medium, a plurality of aggregates deposited on a substrate and lithography produced metal aggregates.

100. A method as in claim 99, wherein the plurality of aggregates comprise clusters of metal particles.

101. A method as in claim 100, wherein the metal particles are selected from the group consisting of silver, gold and copper particles.

102. A method as in claim 99, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

103. A method as in claim 100, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.
104. A method as in claim 96, comprising allowing each fragment to become surface-  
5 absorbed on a plurality of protrusions and voids on a rough metal film.
105. A method as in claim 96, wherein the electromagnetic radiation is non-resonant radiation.
- 10 106. A method as in claim 96, wherein the electromagnetic radiation is near infrared radiation.
107. A method for general field enhancement, comprising providing a plurality of aggregates, exposing the plurality of aggregates to near infrared radiation and inducing at  
15 least one electromagnetic resonance in the plurality of aggregates to cause a surface-enhanced radiation.
108. A method as in claim 107, wherein the near infrared radiation has a wavelength of at least 1000 nm.
- 20 109. A method as in claim 107, wherein the plurality of aggregates comprises a plurality of metal particles.
110. A method as in claim 109, wherein the metal particles are selected from the group  
25 consisting of silver, gold and copper particles.
111. A method as in claim 107, wherein the aggregate is formed in situ by exposure to the electromagnetic radiation.
- 30 112. A method as in claim 107, wherein the plurality of aggregates is selected from the group consisting of colloids suspended in a medium, aggregates deposited on a substrate and lithography produced metal aggregates.

113. A method as in claim 112, wherein the medium is selected from the group consisting of water, an organic solvent and a gel.

114. A method as in claim 112, wherein the substrate is selected from the group consisting of an electrode, a glass layer and a quartz layer.

115. A method as in claim 109, wherein each metal particle has a dimension of no more than about 100 nm.

116. A method as in claim 109, wherein the plurality of aggregates comprises at least seven metal particles.

117. A method as in claim 107, wherein the surface enhanced radiation has an enhancement factor of at least 1010.

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118. A method for selecting a spectral range, comprising:  
providing a sample;  
positioning at least one filter in association with an optical excitation and detection system, wherein the system is free of a spectrograph and the optical excitation system produces electromagnetic radiation in a first range;  
exposing the sample to electromagnetic radiation via the system; and  
obtaining a Raman spectrum of the sample having a second range wherein the second range is shifted from the first range.

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119. A method as in claim 118, involving positioning at least two filters in association with the optical excitation and detection system.

120. A method as in claim 118, the positioning step involving positioning the at least one filter between a sample and detector of a Raman spectral system.

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121. A method as in claim 118, wherein the second range is narrower than the first range.

122. A method for determining the presence of an analyte, comprising:

providing a sample comprising a rough metal film including a plurality of protrusions and indentations;

absorbing a plurality of analytes on a surface of the film;

exposing the sample to electromagnetic radiation to cause Raman scattering; and

5 obtaining a unique Raman signal attributed to a single analyte.

123. A system for determining the presence of at least one analyte, comprising:

a sample;

a source of electromagnetic radiation positioned to irradiate the sample; and

10 a detector positioned to detect surface-enhanced emission from the sample, wherein the sample comprises a plurality of aggregates of size of at least about 500 nm.

124. A system as in claim 123, wherein the sample comprises a plurality of aggregates of size of at least about 500 nm on a substrate.

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